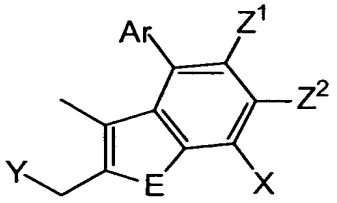
WHAT IS CLAIMED:

1. A method for treatment of Syndrome X or type II diabetes in a mammal, the method comprising administering to a mammal in need thereof:

a) a pharmaceutically effective amount of a biguanide agent; and

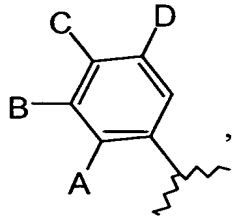
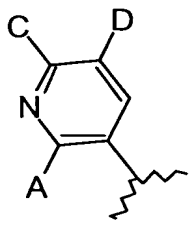
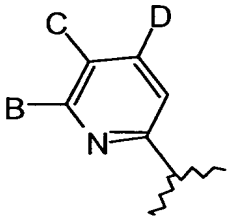
b) a pharmaceutically effective amount of a PTPase inhibiting compound of formula I:



(I)

wherein

Ar is


, 
, or 

A is hydrogen, halogen, or OH;

B and D are each, independently, hydrogen, halogen, CN, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, hydroxyaralkyl of 6-12 carbon atoms, cycloalkyl of 3-8 carbon atoms, nitro, amino, $-NR^1R^{1a}$, $-NR^1COR^{1a}$, $-NR^1CO_2R^{1a}$, cycloalkylamino of 3-8 carbon atoms, morpholino, furan-2-yl, furan-3-yl, thiophen-2-yl, thiophen-3-yl, $-COR^{1b}$ or OR;

R is hydrogen, alkyl of 1-6 carbon atoms, $-COR^1$, $-(CH_2)_nCO_2R^1$, $-CH(R^{1a})CO_2R^1$, $-SO_2R^1$, $-(CH_2)_mCH(OH)CO_2R^1$, $-(CH_2)_mCOCO_2R^1$, $-(CH_2)_mCH{=}CHCO_2R^1$, or $-(CH_2)_mO(CH_2)_oCO_2R^1$;

R^1 is hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, aryl, or $CH_2CO_2R^{1'}$;

$R^{1'}$ is hydrogen or alkyl of 1-6 carbon atoms

E is S, SO, SO_2, O, or NR^{1c};

X is hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-7 carbon atoms, CN, aryl, aralkyl of 6-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, hydroxyaralkyl of 6-12 carbon atoms, perfluoroalkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, aryloxy; arylalkoxy, nitro, amino, NR^2R^{2a}, NR^2COR^{2a}, cycloalkylamino of 3-8 carbon atoms, morpholino, alkylsulfanyl of 1-6 carbon atoms, arylsulfanyl, pyridylsulfanyl, 2-N,N-dimethylaminoethyl-sulfanyl, $-OCH_2CO_2R^{2b}$ or $-COR^{2c}$;

Y is hydrogen, halogen, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, hydroxyaralkyl of 6-12 carbon atoms, $-OR^3$, SR^3, NR^3R^{3a} , $-COR^{3b}$, morpholine or piperidine;

R^{1a}, R^{1c}, R^2, R^{2a} R^3, R^{3a} are each, independently, hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, or aryl;

R^{1b} is alkyl of 1-6 carbon atoms or aryl;

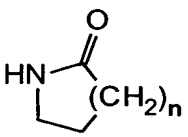
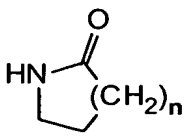
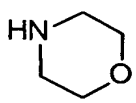
R^{2b} is hydrogen, alkyl of 1-6 carbon atoms;

R^{2c} and R^{3b} are each, independently, alkyl of 1-6 carbon atoms, aryl, or aralkyl of 6-12 carbon atoms;

C is hydrogen, halogen or OR^4 ;

R^4 is hydrogen, alkyl of 1-6 carbon atoms, $-CH(R_5)W$, $-C(CH_3)_2CO_2R^6$, 5-thiazolidine-2,4-dione, $-CH(R^7)(CH_2)_mCO_2R^6$, $-COR^6$, $-PO_3(R^6)_2$, $-SO_2R^6$, $-(CH_2)_pCH(OH)CO_2R^6$, $-(CH_2)_pCOCO_2R^6$, $-(CH_2)_pCH=CHCO_2R^6$, or $-(CH2)_pO(CH_2)_qCO_2R^6$;

R^5 is hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, aryl, $-CH_2$(1H-imidazol-4-yl), $-CH_2$(3-1H-indolyl), $-CH_2CH_2$(1,3-dioxo-1,3-dihydro-isoindol-2-yl), $-CH_2CH_2$(1-oxo-1,3-dihydro-isoindol-2-yl), $-CH_2$(3-pyridyl), $-CH_2CO_2H$, or $-(CH_2)_nG$;

G is $NR^{6a}R^{7a}$, $NR^{6a}COR^{7a}$,  ,  , or  ;

W is CO_2R^6, $CONH_2$, CONHOH, CN, $CONH(CH_2)_2CN$, 5-tetrazole, $-PO_3(R^6)_2$, $-CH_2OH$, $-CONR^{6b}CHR^{7b}$, $-CH_2NR^{6b}CHR^{7b}CO_2R^6$, $-CH_2OCHR^{7b}CO_2R^6$ $-CH_2Br$, or $-CONR^{6b}CHR^{7b}CO_2R^6$;

R^6, R^{6a}, R^7, R^{7a} are each, independently, is hydrogen, alkyl of 1-6 carbon atoms, or aryl;

R^{6b} is hydrogen or $-COR^{6c}$;

R^{6c} is alkyl of 1-6 carbon atoms or aryl;

R^{7b} is hydrogen, alkyl of 1-6 carbon atoms, or hydroxyalkyl of 1-6 carbon atoms;

Z^1 and Z^2 are each, independently, hydrogen, halogen, CN, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, cycloalkyl of 3-8 carbon atoms, nitro, amino, $-NR^1R^{1a}$, $-NR^1COR^{1a}$, cycloalkylamino of 3-8 carbon atoms, morpholino, or OR^8, or Z^1 and Z^2 may be taken together as a diene unit having the formula $-CH=CR^9-CR^{10}=CR^{11}-$;

R^8 is hydrogen, alkyl of 1-6 carbon atoms, or aryl;

R^9, R^{10}, and R^{11} are each, independently, hydrogen, alkyl of 1-6 carbon atoms, aryl, halogen, hydroxy, or alkoxy of 1-6 carbon atoms

m is 1 to 4

n is 1 or 2;

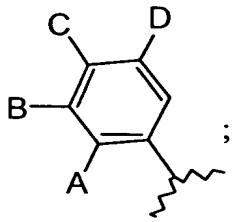
p is 1 to 4;

q is 1 to 4;

or a pharmaceutically acceptable salt thereof; and

c) optionally, a pharmaceutically effective amount of a sulfonylurea agent, or a pharmaceutically acceptable salt form thereof.

2. The method of Claim 1 wherein the PTPase inhibiting compound is as defined in Claim 1, wherein:

Ar is 

;

A is hydrogen or halogen

B and D are each, independently, hydrogen, halogen, CN, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, branched alkyl, cycloalkyl of 3-8 carbon atoms, nitro or OR;

R is hydrogen or alkyl of 1-6 carbon atoms;

E is S, or O;

X is hydrogen, halogen, alkyl of 1-6 carbon atoms, CN, perfluoroalkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, aryloxy; arylalkoxy, nitro, amino, NR^2R^{2a}, NR^2COR^{2a}, cycloalkylamino, morpholino, alkylsulfanyl of 1-6 carbon atoms, arylsulfanyl, pyridylsulfanyl, or 2-N,N-dimethylaminoethylsulfanyl;

R^1, R^{1a}, R^2, R^{2a}, R^3, and R^{3a} are each, independently, hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, or aryl;

Y is hydrogen, halogen, OR^3, SR^3, NR^3R^{3a}, or morpholine;

C is hydrogen, halogen, or OR^4;

R^4 is hydrogen, alkyl of 1-6 carbon atoms, $-CH(R^5)W$, $-C(CH_3)_2CO_2R^6$, 5-thiazolidine-2,4-dione, $-CH(R^7)(CH_2)_mCO_2R^6$, $-COR^6$, $-PO_3(R^6)_2$, $-SO_2R^6$, $-(CH_2)_pCH(OH)CO_2R^6$, $-(CH_2)_pCOCO_2R^6$, $-(CH_2)_pCH=CHCO_2R^6$, $-(CH_2)_pO(CH_2)_qCO_2R^6$;

R^5 is hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, aryl, $-CH_2$(1H-imidazol-4-yl), $-CH_2$(3-1H-indolyl), $-CH_2CH_2$(1,3-dioxo-1,3-dihydro-isoindol-2-yl), $-CH_2CH_2$(1-oxo-1,3-dihydro-isoindol-2-yl), or $-CH_2$(3-pyridyl);

W is CO_2R^6, $-CONH_2$, -CONHOH, 5-tetrazole, or $-CONR^{6b}CHR^{7b}CO_2R^6$;

R^6, R^{6a}, R^{6b}, R^7, R^{7a} , and $R^{7b}$are each, independently, hydrogen, alkyl of 1-6 carbon atoms, or aryl;

Z^1 and Z^2 are each, independently, hydrogen, halogen, CN, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, cycloalkyl of 3-8 carbon atoms, nitro, amino, $-NR^1R^{1a}$, $-NR^1COR^{1a}$, cycloalkylamino of 3-8 carbon atoms, morpholino, or OR^8, or Z^1 and Z^2 may be taken together as a diene unit having the formula $-CH=CR^9-CR^{10}=CH-$;

R^9 and R^{10} are each, independently, hydrogen, or alkyl of 1-6 carbon atoms;
p is 1 to 4;
q is 1 to 4;
or a pharmaceutically acceptable salt thereof.

3. The method of Claim 2 wherein the PTPase inhibiting compound is defined in Claim 2, wherein
A is hydrogen;
B and D are each, independently, halogen, alkyl of 1-6 carbon atoms, aryl, aralkyl of 6-12 carbon atoms, or cycloalkyl of 3-8 carbon atoms;
E is S or O;
X is hydrogen, halogen, alkyl of 1-6 carbon atoms, perfluoroalkyl of 1-6 carbon atoms, CN, alkoxy of 1-6 carbon atoms, aryloxy, arylalkoxy of 6-12 carbon atoms, arylsulfanyl;
Y is hydrogen, $-NR^1R^2$, or morpholine;
R^1 and R^2 are each, independently, hydrogen or alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, or aryl;
C is OR^4;
R^4 is hydrogen, alkyl of 1-6 carbon atoms, $-CH(R^5)W$, or 5-thiazolidine-2,4-dione;
R^5 is hydrogen, alkyl of 1-6 carbon atoms, aralkyl of 6-12 carbon atoms, aryl, $-CH_2$(3-1H-indolyl), $-CH_2CH_2$(1,3-dioxo-1,3-dihydro-isoindol-2-yl), or $-CH_2CH_2$(1-oxo-1,3-dihydro-isoindol-2-yl);
W is $-CO_2R^6$, $-CONH_2$, -CONHOH, 5-tetrazole, $-PO_3(R^6)_2$, or $-CONR^6CHR^6CO_2R^6$;
R^6 is hydrogen or alkyl of 1-6 carbon atoms;
Z^1 and Z^2 are taken together as a diene unit having the formula -CH=CH-H=CH-;
or a pharmaceutically acceptable salt thereof.

4. The method of Claim 1 wherein the PTPase inhibiting compound is (2R)-2-[4-(9-Bromo-2,3-dimethyl-naptho[2,3-*b*]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionic acid, or a pharmaceutically acceptable salt form thereof.

5. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(R)-2-[2,6-dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2-bromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-6-ethyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2, 6-dimethyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-fluoro-phenoxy]-3-phenyl-propionic acid;

[4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2, 6-diisopropyl-phenoxy]-acetic acid;

or a pharmaceutically acceptable salt form thereof.

6. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(R)-2-[2-bromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-6-sec-butyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2-bromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-6-isopropyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2-bromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-cyclopentyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-6-isopropyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-cyclopentyl-phenoxy]-3-phenyl-propionic acid; or a pharmaceutically acceptable salt thereof.

7. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(R)-2-[2,6-dibromo-4-(2,3-dimethyl-9-phenylsulfanyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2,6-dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-4-phenyl-butyric acid;

(S)-2-[2,6-dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-4-phenyl-butyric acid;

2-[2,6-dibromo-4-(9-bromo-3-methyl-2-morpholin-4-ylmethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2,6-dibromo-4-(2,3-dimethyl-9-phenylsulfanyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-propionic acid; or a pharmaceutically acceptable salt thereof.

8. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

[2-bromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-nitro-phenoxy]-3-phenyl-propionic acid;

2, 6-dibromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenol;

2-bromo-4-(9-bromo-2, 3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-6-nitro-phenol;

(R)-2-[2,6-dibromo-4-(9-bromo-2-diethylaminomethyl-3-methyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2,6-dibromo-4-(2,3-dimethyl-naphtho[2,3-b]furan-4-yl)-phenoxy]-3-phenyl-propionic acid; or a pharmaceutically acceptable salt thereof.

9. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(2R)-2-[4-9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diisopropyl-phenoxy]-3-phenyl-propionic acid,

(R)-2-[4-(9-bromo-2-,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionic acid;

{(2R)-2-[4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionylamino}-acetic acid;

{(2R)-2-[4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionylamino}-acetic acid;

(2R)-2-[4-(9-Bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-3-phenyl-propionic acid; or a pharmaceutically acceptable salt thereof.

10. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(2S)-2-[4-(9-Bromo-2-,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionic acid;

{(2R)-2-[4-(2,3-Dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionylamino}-acetic acid;

(R)-2-[4-(9-Bromo-2-,3-dimethyl-naphtho[2,3-b]furan-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[2-Cyclopentyl-4-(2-,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]-propionic acid;

(R)-2-[4-(9-Bromo-2-,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-cyclopentyl-phenoxy]-propionic acid; or a pharmaceutically acceptable salt thereof.

11. The method of Claim 1 wherein the PTPase inhibiting compound is selected from the group of:

(R)-2-[4-(2-,3-Dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-ethyl-phenoxy]-3-phenyl-propionic acid;

2-Bromo-4-(2-,3-dimethyl-naphtho[2,3-b]furan-4-yl)-6-ethyl-phenol;

(R)-2-[2-Bromo-4-(2-,3-dimethyl-naphtho[2,3-b]furan-4-yl)-6-ethyl-phenoxy]-3-phenyl-propionic acid;

(R)-2-[4-(9-Bromo-2-,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2-propyl-phenoxy]-3-phenyl-propionic acid;

(2R)-2-[4-(9-Bromo-2-diethylaminomethyl-3-methyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diisopropyl-phenoxy]-3-phenyl-propionic acid;

or a pharmaceutically acceptable salt thereof.

12. The method of Claim 1 wherein the biguanide agent is metformin, or a pharmaceutically acceptable salt thereof.

13. The method of Claim 1 wherein the optional sulfonylurea agent is selected from group of glyburide, glyburide, glipizide, glimepiride, chlorpropamide, tolbutamide, or tolazamide, or a pharmaceutically acceptable salt form thereof.

14. A method of treating metabolic disorders mediated by insulin resistance or hyperglycemia in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a pharmaceutically effective amount of a PTPase inhibiting compound, as described in Claim 1, a pharmaceutically effective amount of a biguanide agent and, optionally, a sulfonylurea agent and or a pharmaceutically acceptable salt thereof.

15. The method of Claim 14 wherein the biguanide agent is metformin, or a pharmaceutically acceptable salt thereof.

16. The method of Claim 14 wherein the optional sulfonylurea agent is selected from group of glyburide, glyburide, glipizide, glimepiride, chlorpropamide, tolbutamide, or tolazamide, or a pharmaceutically acceptable salt form thereof.

17. The method of Claim 14 wherein the PTPase inhibiting compound is (2R)-2-[4-(9-Bromo-2,3-dimethyl-naptho[2,3-*b*]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionic acid, or (R)-2-[2,6-Dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]3-phenyl-propionic acid, or (R)-2-[4-(9-Bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionic acid, or a pharmaceutically acceptable salt form thereof.

18. A method of modulating blood glucose levels in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a pharmaceutically effective amount of a PTPase inhibiting compound, as described in Claim 1, a pharmaceutically effective amount of a biguanide agent and, optionally, a sulfonylurea agent and or a pharmaceutically acceptable salt thereof.

19. The method of Claim 18 wherein the biguanide agent is metformin, or a pharmaceutically acceptable salt thereof.

20. The method of Claim 18 wherein the optional sulfonylurea agent is selected from group of glyburide, glyburide, glipizide, glimepiride, chlorpropamide, tolbutamide, or tolazamide, or a pharmaceutically acceptable salt form thereof.

21. The method of Claim 18 wherein the PTPase inhibiting compound is (2R)-2-[4-(9-Bromo-2,3-dimethyl-naptho[2,3-*b*]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionic acid, or (R)-2-[2,6-Dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]3-phenyl-propionic acid, or (R)-2-[4-(9-Bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionic acid, or a pharmaceutically acceptable salt form thereof.

22. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and:

a) a pharmaceutically effective amount of metformin, or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically effective amount of a PTPase inhibiting compound of Claim 1, or a pharmaceutically acceptable salt form thereof; and

c) optionally, a pharmaceutically effective amount of a sulfonylurea agent.

23. The pharmaceutical composition of Claim 22 comprising a pharmaceutically acceptable carrier or excipient and:

a) a pharmaceutically effective amount of metformin, or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically effective amount of (2R)-2-[4-(9-Bromo-2,3-dimethyl-naptho[2,3-*b*]thiophen-4-yl)-2,6-dimethyl-phenoxy]-3-phenyl-propionic acid, or (R)-2-[2,6-Dibromo-4-(9-bromo-2,3-dimethyl-naphtho[2,3-b]thiophen-4-yl)-phenoxy]3-phenyl-propionic acid, or (R)-2-[4-(9-Bromo-2,3-dimethyl-naphtho[2,3-b]-thiophen-4-yl)-2,6-diethyl-phenoxy]-3-phenyl-propionic acid, or a pharmaceutically acceptable salt form thereof; and

c) optionally, a pharmaceutically effective amount of a sulfonylurea agent selected from the group of glyburide, glyburide, glipizide, glimepiride,

chlorpropamide, tolbutamide, or tolazamide, or a pharmaceutically acceptable salt form thereof.